Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Thus, the specification has been amended in response to the objection to the disclosure in item 1 on page 2 of the Office Action, rendering the objection moot.

Claim 1 has been amended to incorporate the subject matter of claim 7, and to indicate that the inorganic acid is phosphoric acid, which is taken from claim 4. Amended claim 1 also specifies that the amount of the water-soluble polymer is 0.15 to 5.0 wt% based on the weight of the preparation, which is supported by page 11, line 21 of the specification. Furthermore, amended claim 1 specifies that the pH of the preparation in the form of a solution just before gelation is 6.0 or more and 7.4 or less, which is based on page 13, lines 1-4.

Claim 2 has been amended to be consistent with amended claim 1 with respect to the inorganic acid.

Claims 3-5, 7 and 9 have been cancelled, in view of the amendments to claim 1.

Claim 6 has been amended to depend on claim 1 in view of the cancellation of claim 5.

New claim 10 has been added to the application, and is supported by page 9, lines 6-9 of the specification.

The Examiner's comment in item 2 on page 2 of the Office Action has been adopted in amending claim 1.

The patentability of the presently claimed invention after entry of the foregoing amendments, over the disclosures of the references relied upon by the Examiner in rejecting the claims, will be apparent upon consideration of the following remarks.

Initially, the rejection of claims 1-6, 8 and 9 under 35 U.S.C. §103(a) as being unpatentable over Nishii et al. (WO '320) in view of Sequeira et al. (US '711) has been rendered moot in view of the claim amendments. That is, as indicated above, the subject matter of claim 7, which is not subject to this rejection, has been incorporated into claim 1.

The rejection of claims 1-3 and 7-9 under 35 U.S.C. §103(a) as being unpatentable over Nishii et al. and Sequeira et al. further in view of Hart et al. (US '134) is respectfully traversed.

The oral formulation of Nishii et al. contains a biguanide and an organic acid (claim 1), and the pH of the formulation (solution) is 3.5 to 6 (claim 9).

A jelly formulation is described in Nishii et al. in Example 9, and the formulation contains gelatin as a binder (page 4, lines 17 to 20). The examples of the binder are hydroxypropylcellulose, hydroxypropylmethylcellulose, polyvinylpyrrolidone, gelatin, methylcellulose, Arabia gum and polyvinylalcohol (page 4, lines 17 to 20).

On the other hand, the preparation of the present invention contains a biguanide drug, phosphoric acid, and a specified water-soluble polymer, and the pH of the preparation (solution) is 6.0 or more and 7.4 or less.

As apparent from the disclosures in the present specification in the paragraph bridging pages 3-4 and the first full paragraph on page 5, the jelly formulation described in Nishii et al. is not easily gelled because of the addition of the organic acid. When the gelatin concentration was increased to accelerate gelling while an organic acid was added, the ability for releasing the drug was decreased.

The objective of the invention described in Nishii et al. is to control unpleasant tastes (page 1, line 29 to page 2, line 4) and to have the biguanide included in the formulation in a stable manner (Experiment 2). However, the stability of the preparation itself and the releasability of the biguanide are not considered in Nishii et al.

On the other hand, it is an objective of the present invention to provide a biguanide drug-containing jelly preparation for which discomfort on administration is decreased, and which has excellent stability and also releasability of the biguanide drug (page 5, lines 21-25 of the present specification).

Especially, the preparation of the present invention contains phosphoric acid as the agent for masking the bitter taste of the biguanide drug, and the pH is 6.0 or more. As a result, the bitter taste of the biguanide drug is decreased, while the preparation is stable (page 18, lines 4-19 of the present specification). Further, the preparation of the present invention has excellent releasability of the biguanide drug (Test Example 1 of the present specification), and the preparation is stable.

The Examiner recognizes that Nishii et al. do not disclose the use of inorganic acids, such as the phosphoric acid recited in amended claim 1. The Examiner takes the position that it would have been obvious to use an inorganic acid in lieu of the organic acid used by Nishii et al. as Sequeira et al. disclose that inorganic acid systems such as phosphoric acid and sodium phosphate monobasic are useful in maintaining the pH of jelly drug formulations.

However, there is no suggestion in the references which would lead one of ordinary skill in the art to expect that the inorganic acids of Sequeira et al. would be equivalent to the organic acids of Nishii et al. Accordingly, Applicants respectfully submit that, contrary to the position taken by the Examiner, one of ordinary skill in the art would not have used an inorganic acid in lieu of the organic acid used by Nishii et al. Furthermore, even if the Examiner has established a presumption that it would be obvious to make this substitution of inorganic acid for organic acid, such presumption has been overcome by the unexpected superior results achieved by the present invention, as discussed above, when using phosphoric acid in place of the organic acid of Nishii et al.

Furthermore, Applicants note that the pharmaceutical composition of Sequeira et al. contains an antiandrogen compound and a gelling agent, and the pH of the composition is 5 or less (claim 1). The pharmaceutical composition is used for topical treatment (claim 1), and is not used orally. The example of the gelling agent is alkyl- and hydroxyalkyl ethers such as hydroxyethylcellulose, and carboxypolymethylene such as carboxyvinylpolymer (column 3, lines 46 to 54).

On the other hand, the preparation of the present invention contains a biguanide drug, which is basic, and is different from the antiandrogen compound which is neutral; the preparation of the present invention is orally administered; and the pH of the preparation of the present invention is 6.0 or more and 7.4 or less.

The formulation of Nishii et al. is orally administered, while the pharmaceutical composition of Sequeira et al is topically administered; the biguanide drug used in Nishii et al. is basic and is used for the treatment of diabetes, while the antiandrogen compound in Sequeira et al. is neutral and is used for the treatment of androgen-related disorders.

In view of these differences between Nishii et al. and Sequeira et al., Applicants take the position that one of ordinary skill in the art would not combine these references in the manner suggested by the Examiner.

In addition, the pH of the formulation of Nishii et al. is 3.5 to 6, and the pH of the composition of Sequeira et al. is 5 or less, while the pH of the preparation of the present invention is 6.0 or more and 7.4 or less. Further, the gelling agents described in Nishii et al. and Sequeira et al. are different from the specified water-soluble polymer of the present invention.

The Examiner recognizes that neither Nishii et al. nor Sequeira et al. disclose the use of any of the water-soluble polymers specified in claim 7 of the present application, which has now been incorporated into amended claim 1. The Examiner takes the position that Hart et al. disclose gelling agents which include some of those specified in amended claim 1, and that it would have been obvious to use a water-soluble polymer as taught by Hart et al. as functionally equivalent to the gelatin used in the composition of Nishii et al.

Hart et al. describe locust bean gum (claims 1 and 6). [Locust bean gum is the same as carob bean gum.] However, the locust bean gum is depolymerized (claims 1 and 6). The depolymerized locust bean gum is different from carob bean gum itself.

With regard to the Examiner's position that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use another water-soluble polymer such as carrageenan or locust bean gum, taught by Hart et al. as functionally equivalent to the gelatin, the gelling agent composition of Hart et al. indispensably contains depolymerized locust bean gum. On the other hand, the water-soluble polymer contained in the preparation of the present invention is a polymer, and thus is not depolymerized.

In summary, Applicants take the position that the preparation of the present invention is completely different from those described in the references. Especially, the preparation of the present invention is characterized in that phosphoric acid is contained therein for masking the bitter taste of the biguanide drug, and the pH is 6.0 or more and 7.4 or less. Such a preparation is not described in the references. In the present invention, the stability of the preparation itself, not only the biguanide drug, is improved, while the bitter taste of the biguanide drug is masked, owing to the inclusion of phosphoric acid in the preparation and the pH of the preparation adjusted in the range of 6.0 or more and 7.4 or less. On the other hand, the stability of the preparation itself is not considered in the references although the stability of the contained drug is considered. In addition, the preparation of the present invention has excellent releasability of the biguanide drug (Test Example 1 of the present application), and the preparation is stable.

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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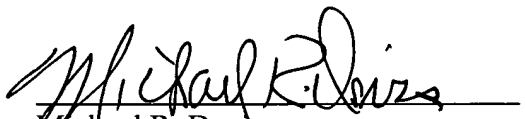
By: 

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